

Serial No.: 09/897,465  
Amendment dated 12 September 2003  
Reply to Office Action mailed 12 March 2003

### REMARKS

The specification has been amended so that the description on page 7, line 9 is consistent with the description on page 7, lines 11-14.

Claims 2, 9-12 and 16-18 have been canceled. Claim 1 has been amended to limit it to the elected species, namely PnIA[A10L] of SEQ ID NO:10. Claim 1 has further been amended to include the subtype specificity of PnIA[A10L], namely  $\alpha 7$  and  $\alpha 3\beta 2$ . Support for this latter limitation can be found at page 6, lines 36-37, which discloses that the  $\alpha$ -conotoxins of the invention are active on the  $\alpha 3\beta 4$ ,  $\alpha 3\beta 2$  or  $\alpha 7$  subtypes of neuronal nicotinic acetylcholine receptors (nAChRs) and at page 7, lines 7-11, which discloses that PnIA[A10L] has higher specificity for the  $\alpha 7$  subtype of nAChRs. Since it has higher specificity for the  $\alpha 7$  subtype of nAChRs, it must necessarily also have specificity to the  $\alpha 3\beta 2$  subtype of nAChRs. Claims 13 and 14 have been amended to change their dependency. Claim 14 has further been amended to clarify that a Tyr, mono-iodo-Tyr or di-iodo-Tyr residue is added at the N-terminus of PnIA[A10L] and becomes the new N-terminus. Claim 15 has been amended to indicate that this residue is Tyr. New claims 19 and 20 have been added to indicate that this residue is mono-iodo-Tyr or di-iodo-Tyr, respectively. New claims 21-32 have been added to depend from claims 13 and 14 and correspond to original claims 3-8.

It is submitted that these amendments do not constitute new matter, and their entry is requested.

Claims 12-15 were objected to for reading on non-elected subject matter. The amendment of the claims obviates this objection.

Claims 1-8 and 11-14 were rejected under 35 U.S.C. §112, first paragraph for lack of enablement with respect to the treatment of specific disorders with PnIA[A10L]. Applicants have amended claim 1 to specify that the disorders which are treated are those that are regulated at the  $\alpha 7$  or  $\alpha 3\beta 2$  subtypes of nAChRs. As discussed above with respect to the claim amendments, support for this activity of PnIA[A10L] can be found at page 6, line 36 - page 7, line 11. This passage discloses that the  $\alpha$ -conotoxins of the present invention are useful for treating various disorders regulated at the  $\alpha 7$ ,  $\alpha 3\beta 2$  or  $\alpha 3\beta 4$  subtypes of nAChRs. This passage further discloses that the  $\alpha$ -

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conotoxins can be designed to be more specific for one of these subtypes. i.e., they are more specific for one of the subtypes but still show activity with respect to other subtypes. For example, PnIA has a higher specificity for the  $\alpha 3\beta 2$  subtype of nAChRs, whereas PnIA[A10L] has a higher specificity for the  $\alpha 7$  subtype of nAChRs. Since PnIA[A10L] has a higher specificity for the  $\alpha 7$  subtype of nAChRs, it necessarily also has specificity to the subtype of the unmodified  $\alpha$ -conotoxin, PnIA, i.e., the  $\alpha 3\beta 2$  subtype of nAChRs. In fact, PnIA[A10L] acts with highest potency on  $\alpha 7$  nAChRs ( $IC_{50} = 12$  nM) but binds to  $\alpha 3\beta 2$  nAChRs with about 8-times less potency ( $IC_{50} = 99$  nM).

In view of these remarks and the amendment of the claims, it is submitted that the specification fully enables the claimed subject matter, i.e., the treatment of disorders that are regulated at the  $\alpha 7$  or  $\alpha 3\beta 2$  subtypes of nAChRs. Withdrawal of this rejection is requested.

Claims 14 and 15 were rejected under 35 U.S.C. §112, second paragraph for being indefinite. It is submitted that the amendments to these claims obviate this rejection. Withdrawal of this rejection is requested.

Claims 1 and 6 were rejected under 35 U.S.C. §102(e) as being anticipated by McIntosh et al. (US 5,780,433). It is submitted that the amendment of claim 1 obviates this rejection. Withdrawal of this rejection is requested.

Claims 1 and 7 were rejected under 35 U.S.C. §102(e) as being anticipated by McIntosh et al. (US 5,929,034). It is submitted that the amendment of claim 1 obviates this rejection. Withdrawal of this rejection is requested.

Claims 1 and 7 were rejected under 35 U.S.C. §102(e) as being anticipated by McIntosh et al. (US 5,922,679). It is submitted that the amendment of claim 1 obviates this rejection. Withdrawal of this rejection is requested.

Claims 1 and 6 were rejected under for obviousness-type double patenting over claims 1-5 of U.S. Patent No. 5,780,433. It is submitted that the amendment of claim 1 obviates this rejection. Withdrawal of this rejection is requested.

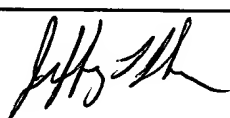
Claims 1 and 7 were rejected for obviousness-type double patenting over claims 1-5 of U.S. Patent No. 4,780,433. Applicants note that this cited patent is not related to the subject matter of the

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present application and that the Examiner may have meant to refer to U.S. Patent No. 5,929,034. It is submitted that the amendment of claim 1 obviates this rejection. Withdrawal of this rejection is requested.

Claims 1 and 7 were rejected for obviousness-type double patenting over claims 1-6 of U.S. Patent No. 5,922,679. It is submitted that the amendment of claim 1 obviates this rejection. Withdrawal of this rejection is requested.

In view of the above amendments and remarks, it is submitted that the present claims satisfy the requirements of the patent statutes and are patentable over the prior art. Reconsideration and early notice of allowance are requested. The Examiner is invited to telephone the undersigned in order to expedite prosecution of the present application.

RESPECTFULLY SUBMITTED,					
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